Amendments to the specification

Please replace paragraph 1 at page 1 with the following amended paragraph.

[0001] This application is a continuation-in-part of application and claims priority of pending U.S. application Serial No. 10/651,515, filed August 28, 2003, which ~~is a continuation-in-part of~~ claims priority from abandoned U.S. provisional application Serial No. 60/407,146, filed August 28, 2002, abandoned U.S. provisional application Ser. No. 60/408,332, filed September 4, 2002, and ~~pending~~ abandoned U.S. provisional application Ser. No. 60/479,257, filed June 17, 2003, all of which are incorporated herein by reference.

Please replace paragraph 15 at page 6 with the following amended paragraph.

[0015] The methods include a method to prevent, treat, ameliorate or slow the progression of cystic fibrosis, sickle cell disease, ~~neutropenia or thrombocytpoenia~~ neutropenia or thrombocytopenia in a subject, or to treat a symptom of the cystic fibrosis, sickle cell disease, neutropenia or thrombocytopenia, comprising administering to a subject, or delivering to the subject's tissues, an effective amount of a formula 1 compound having the structure 5, 6, 7, 8, 9, 10, 11, 12, 13 or 14

Please replace paragraph 30 at page 8 with the following amended paragraph.

[0030] R^{PR} independently is -H or a protecting group. In typical embodiments, one or two of R^{10A}, R^{10B}, R^{10C}, R^{10D} and R^{10E} are not hydrogen or one R^4 is $-NH_2$, an ~~opotionally substituted amine,~~ optionally substituted

amine, $-N(R^{PR})^2$, =NOH, =NO-optionally substituted alkyl, an amide or an N-linked amino acid.

Please replace paragraph 57 at page 17 with the following amended paragraph.

[0057] "Substituted alkyl", "substituted alkenyl", "substituted alkynyl", substituted alkylaryl", "substituted arylalkyl", "substituted heterocycle", "substituted aryl", "substituted monosaccharide" and the like mean an alkyl, alkenyl, alkynyl, alkylaryl, arylalkyl heterocycle, aryl, monosaccharide or other group or moiety as defined or disclosed herein that has a substituent(s) that replaces a hydrogen atom(s) or a substituent(s) that interrupts a carbon atom chain. Substituted heterocycles may thus have a substituent bonded to a ring carbon or a ring heteroatom such as a nitrogen. Substituents for any of these moieties include 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 or more independently selected -O-, -S-, -NH-, -C(O)-, -C(O)OH, $-C(O)OR^{15A}$, $-C(O)OR^{PR}$, $-C(O)SR^{15A}$, $-C(O)SR^{PR}$, -CHO, -CHS, $-CH_2SH$, -C=N-, -OH, =O, $-OR^{15A}$, $-OR^{PR}$, $-C(O)OR^{PR}$, -O-C(O)H, $-C(O)CH_3$, $-C(S)CH_3$, -C(S)SH, $-C(S)SR^{15A}$, $-C(S)SR^{PR}$, $-C(O)CH_2OH$, $-C(O)CH_2F$, $-C(O)CH_2Cl$, $-C(O)CH_2Br$, $-C(O)CH_2I$, $-C(O)CF_2H$, $-C(O)CF_3$, $-C(O)NHCH_3$, $-C(O)NHC_2H_5$, $-C(O)NHC(CH_3)_3$, $-O-CH_2-C(O)-C(CH_3)_3$, $-C(O)-C(CH_3)_3$, $-O-CH(CH_3)-O-C(CH_3)_3$, -C(O)O-, $-C(S)OR^{PR}$, -C(S)O-, -OC(O)-, -C(O)H, $-OCH_2-$, $-CH_2-O-CH_2-$, $-(CH_2)_{1-2}-O-(CH_2)_2$, $-OCH_2CH_2-$, $-OCH_2O-$, $-OCH_2CH_2O-$, $-CH_2OH$, $-CH_2F$, $-CHF_2$, $-CF_3$, $-CH_2Cl$, $-CH_2Br$, $-CH_2I$, $-C_2H_4Cl$, $-C_2H_4Br$, $-C_2H_4I$, $-CH_2CH_2F$, $-CH_2CHF_2$, $-CH_2CF_3$, $-NH_2$, $-NHR^{15A}$, $-N(R^{15A})_2$, $-N(R^{PR})_2$, $-NHR^{PR}$, -NHC(O)-, $-CH_2-NR^{PR}-$, $-CH_2-NHR^{PR}$, $-CH_2-NHC(O)-$, -C(O)NH-, $-C(O)NHR^{PR}$, $-OC(O)NR^{PR}-$, $-OC(O)NHR^{PR}$, $-C(=NH)-NH_2$, -C(=NH)OH, $-C(=N-NH_2)OH$, -C(O)NHOH, =NOH, $=NOCH_3$, $=NOC_2H_5$, $=NOC_3H_7$, $=NOC_4H_9$, $-NHR^{15A}$, $=NR^{15A}$, =N-, $-NR^{PR}C(O)NR^{PR}-$, $-NR^{PR}C(O)NHR^{PR}$, $-NR^{PR}CH_2-$, $-NR^{PR}CH_2CH_2-$, $-NO_2$, $-ONO_2$, -S-, -SH, $-SR^{15A}$, $-SR^{PR}$, =S, $-S(O)R^{15A}$, $-S(O)OR^{15A}$, -S(O)-, -S(O)(O)-, $-O-S(O)(O)-NR^{PR}-$, $-O-S(O)(O)-NR^{PR}-CH_2-$, $-CH_2-O-S(O)(O)-NR^{PR}-$, $-CHR^{15A}-S(O)(O)-NR^{PR}-$, -

CHR^{15A}-S(O)(O)-NR^{PR}-CHR^{15A}-, -NH-S(O)(O)H, -CH_2-NH-S(O)(O)H, -CHR^{15A}-NH-S(O)(O)H, -O-S(O)(O)-CHR^{15A}-, -CHR^{15A}-O-S(O)(O)-, -CHR^{15A}-O-S(O)(O)-CHR^{15A}-, -S(O)(O)H, -CHR^{15A}-S(O)(O)H, -NH-S(O)(O)-NH-, -CHR^{15A}-NH-S(O)(O)-NH-, -CHR^{15A}-NH-S(O)(O)-NH-CHR^{15A}, -NH-S(O)(O)-NHR^{PR}, -NH-S(O)(O)-NH_2, -NH-S(O)(O)-$NHCH_3$, -NH-S(O)-NH-, -CHR^{15A}-NH-S(O)-NH-, -CHR^{15A}-NH-S(O)-NH-CHR^{15A}, -NH-S(O)-NHR^{PR}, -NH-S(O)-NH_2, -NH-S(O)-$NHCH_3$, -NH-S(O)-, -CHR^{15A}-NH-S(O)-, -NH-S(O)-CHR^{15A}, -S(O)-NHR^{PR}, -S(O)-NH_2, -S(O)-$NHCH_3$, -S(O)(O)-O-, -S(O)OR^{PR}, -S(O)(O)OH, -OSO_3H_2, -S(O)(O)OR^{15A}, -S(O)(O)OR^{PR}, -S(O)OH, -S(O)OR^{15A}, -S(O)OR^{PR}, -S(O)R^{15A}, -S(O)R^{PR}, -CN, -SCN, -C(O)OH, -C(O)OR^{15A}, -C(O)OR^{PR}, -C(O)SH, -C(O)SR^{15A}, -C(O)SR^{PR}, -C(S)OH, -C(S)OR^{15A}, -C(S)OR^{PR}, -O-P(O)(O)OH, -O-P(O)(O)OR^{15A}, -O-P(O)(O)OR^{PR}, -O-P(S)(O)OH, -O-P(S)(O)OR^{15A}, -O-P(S)(O)OR^{PR}, -O-P(O)(O)SH, -O-P(O)(O)SR^{15A}, -O-P(O)(O)SR^{PR}, -F, -Cl, -Br, -I, -C=NH, -C=NCH_3, -C=NC_2H_5, -C(=S)-, -C_6H_5, -$CH_2C_6H_5$, -O-A8, -S-A8, -C(O)-A8, -OC(O)-A8, -C(O)O-A8, -$OPO_3(R^{PR})_2$, -amino acid-, -O-monosaccharide, -O-disaccharide, -S-monosaccharide, -S-disaccharide, a polymer, e.g., a PEG, and combinations of these moieties and salts on any of these moieties that can form a salt, ~~where where each~~ where each R^{PR} independently is -H, an independently selected protecting group or both R^{PR} together are a protecting group, A8 is C1-C10 optionally substituted alkyl, and R^{15A} independently are -H, -CH_3, -C_2H_5, -C_3H_7, -C_4H_9, -$C(CH_3)_3$, -CH_2OH, -C_2H_4OH, -C_3H_6OH, -C_4H_8OH -$C(CH_2OH)(CH_3)_2$, -C_3H_5, -C_4H_7, optionally substituted C1-10 alkyl, C1-10 perfluoroalkyl, optionally substituted aryl, optionally substituted C1-12 alkylaryl, optionally substituted C1-12 arylalkyl, optionally substituted allyl, optionally substituted heterocycle, optionally substituted C1-4 alkyl-optionally substituted heterocycle or optionally substituted heterocycle-optionally substituted C1-4 alkyl. Substituents are independently chosen when more than one is present. Alkenyl and alkynyl groups that comprise a substituent(s), are optionally substituted at a carbon that is one or more methylene moiety removed from the double bond, e.g., the substituent is optionally separated by one, two, three or more independently

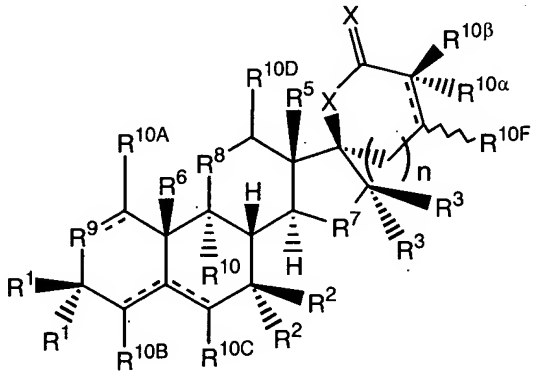
selected -CH_2-, -CH(C_{1-6} optionally substituted alkyl)-, -CH(C_{1-6} optionally substituted alkenyl)-, -CH(C_{1-6} optionally substituted alkynyl)-, -CH(optionally substituted heterocycle)-, -CH(optionally substituted aryl-optionally substituted alkyl)- or -CH(optionally substituted alkyl-optionally substituted aryl)- moieties. Other substituted alkenyl and alkynyl moieties include =CHOH, =CH-halogen, =CH-$COOR^{PR}$, =CH-$(CH_2)_m$-NH_2, =CH-$(CH_2)_m$-NH(C1-C6 alkyl), =CH-N(C1-C6 alkyl)$_2$, =CH-CH_2OH, =CH-CH_2-halogen, =CH-CH_2-$COOR^{PR}$, =CH-CH_2-NH_2, =CH-CH_2-NH(C1-C6 alkyl), =CH-CH_2-N(C1-C6 alkyl)$_2$, =CH-CH_2-CH_2OH, =CH-CH_2-CH_2-halogen, =CH-CHOH-CH_3, =CH-CHOH-CH_2-CH_3,.=CH-CH_2-CH_2-$COOR^{PR}$, =CH-CH_2-CH_2-NH_2, =CH-CH_2-CH_2-N(C1-C4 alkyl)$_2$, -CH=CH-$(CH_2)_m$-OH, -CH=CH-halogen, -CH=CH-CH_2OH, -CH=CH-CH_2-halogen, -C≡C-halogen, -C≡C-CH_2-NH_2, -C≡C-CH_2-NH(C1-C6 alkyl), -C≡C-CH_2-N(C1-C6 alkyl)$_2$, -C≡C-OH, -C≡C-$COOR^{PR}$, -C≡C-CH_2-halogen, -C≡C-CH_2-OH and -C≡C-CH_2-$COOR^{PR}$, where each alkyl moiety is the same or different, e.g., both are methyl, ethyl or propyl or one is methyl and the other is ethyl, propyl or butyl and m is 1, 2, 3 or 4. The organic moieties and substitutions described here, and for other any other moieties described herein, usually will exclude obviously unstable moieties, e.g., -O-O-, except where such unstable moieties are transient species that one can use to make a compound such as a F1C with sufficient chemical stability for the one or more of the uses described herein.

Please replace paragraph 143 at page 42 with the following amended paragraph.

[00143] Embodiments of formula 1 compounds. For formula 1 compounds ("F1Cs"), 2, 3 or more of R^1, R^2, R^3 and R^4 are usually not -H, and typically one or both R^1 and R^4, R^3 and R^4, R^2, R^3 and R^4 or R^2 and R^4 are not -H, and/or 1 or 2 of R^{10A}, R^{10B}, R^{10C} and R^{10D} are optionally not -H. ~~For any F1C disclosed herien~~ For any F1C disclosed herein, steroid nucleus carbon atoms that contain two variable groups (e.g., two R^{10} at R^8 or R^9 or two R^3 or

R^4 at the 16- or 17-position), each variable group is independently selected and each can thus be the same or different, e.g., both can be methyl, ethyl, methoxy, ethoxy, -F, -Cl, -Br, -I, or they can be different. As is apparent from the F1C structures, a double bond can be present at either the 4-5 position or at the 5-6 position, but not at both positions at the same time. Steroid nucleus carbon atoms refers generally to the carbons that make up the rings in F1Cs and carbons, if present, that are bonded to the 10, 13 and 17 positions. Additional carbons that may be at the 17-position are typically numbered using the cholesterol numbering system, although any other suitable nomenclature can be used to describe species or genera of F1C. Exemplary F1C embodiments are described below.

Please replace paragraph 169 at page 48 with the following amended paragraph.



[00169] where X independently are O or S, typically both X are O, $R^{10\alpha}$ is an independently selected R^{10} moiety in the α-configuration, or if a double bond is present, $R^{10\alpha}$ is absent, $R^{10\beta}$ is an independently selected R^{10} moiety in the β-configuration, R^{10F} is an independently selected R^{10} moiety in the α- or β-configuration, n is 0, 1 or 2, and remaining variable groups are as defined above. These compounds include ones where R^1 in the α- and β-configurations independently are an R^1 moiety such as H, OH, halogen, an optionally substituted monosaccharide, an optionally substituted disaccharide or a dicarboxylic acid ester such as -OC(O)-$(CH_2)_2$-COOH, -OC(O)-$(CH_2)_3$-COOH or -OC(O)-$(CH_2)_4$-COOH, R^2 in

the α- and β-configurations independently are an R^2 moiety such as -H, -OH, =O, -SH, =S, halogen, optionally substituted alkyl, a monosaccharide or a disaccharide, R^5 is C1-C4 alkyl, R^6 is -H, halogen or C1-C4 alkyl or R^7 and R^8 independently are moieties as previously defined such as independently selected $-CH_2-$, $-CH(\alpha\text{-}OR^{PR})-$, $-CH(\beta\text{-}OR^{PR})-$, -C(O)- or -O-, R^9 is ~~a moiety as perviously defined~~ a moiety as previously defined such as $-CH_2-$, $-CH(\alpha\text{-halogen})-$, $-CH(\alpha\text{-OH})-$, $-CH(\alpha\text{-optionally substituted alkyl})-$, $-C(halogen)_2-$, $-C(\beta\text{-optionally substituted alkyl})(\alpha\text{-OH})-$, $-CH(\alpha\text{-optionally substituted alkyl})-$, R^{10} at the 9-position is a R^{10} moiety such as -H, -F, -Cl, or optionally substituted alkyl, R^{PR} is -H or a protecting group such as an ester or optionally substituted alkyl and other variable groups are as previously defined. For any of these compounds, 1, 2, 3 or 4 of R^{10A}, R^{10B}, R^{10C} and R^{10D} may be substituted, or they all be -H, while R^{17} may be a moiety defined previously such as C1-C6 optionally substituted alkyl, e.g., $-CH_3$ or $-C_2H_5$.

Please replace paragraph 229 at page 63 with the following amended paragraph.

[00229] When adjacent variable groups are an epoxide or ~~an optiopnally~~ an optionally substituted cyclopropyl ring exemplary F1C structures include

Please replace paragraph 243 at page 65 with the following amended paragraph.

[00243] For these exemplary formula B, C, D, E, F and G structures and any ~~other FiC strutures disclosed herein~~ other F1C structures disclosed herein each R^1, R^{1A}, R^2, R^{2A}, R^3, R^{3B}, R^4, R^{4A}, R^{10}, R^{10A}, R^{10B}, R^{10C}, R^{10D}, R^{10E}, R^{10F} and R^{10G} are an independently selected atom or moiety as described herein, e.g., -H, -OH, =O, -SH, =S, -F, -Cl, -Br, -I, -CN, -SCN, $-N_3$, -NH-C1-C8 optionally substituted alkyl, -N(C1-C8 optionally substituted alkyl)$_2$ where each optionally substituted alkyl moiety is the same or different, protected ketone,

e.g., ethylene ketal (-O-CH_2-CH_2-O-), -NO_2, -ONO_2, -$(CH_2)_n$-CH(O), -$(CH_2)_n$-COOH, -$(CH_2)_n$-$COOR^{PR}$, -$(CH_2)_n$-$NHCH_3$, -$(CH_2)_n$-NHR^{PR}, -$(CH_2)_n$-CH(S), -O-S(O)(O)-OH, -O-P(O)(O)-OH, where n is 0, 1, 2, 3, 4, 5 or 6, -O-β-D-glucopyranosiduronate, -OP(O)(OH)-NH-C(=NH)-N(CH_3)-CH_2-C(O)OH, or a group such as:

Please replace paragraph 251 at page 70 with the following amended paragraph.

[00251] thioester, e.g., -SC(O)CH_3, -SC(O)C_2H_5, -SC(O)C_3H_7, -SC(O)C_4H_9, -SC(O)C_6H_5, -SC(O)$CH_2C_6H_5$, -C(O)SCH_3, -CS(O)C_2H_5, -CS(O)C_3H_7, -CS(O)C_4H_9, -CS(O)C_6H_5, -CS(O)$CH_2C_6H_5$, -S-C(O)-$(CH_2)_2$-C(O)OH, -S-C(O)-$(CH_2)_2$-C(O)OR^{PR}, -S-C(O)-$(CH_2)_3$-C(O)OH, -S-C(O)-$(CH_2)_3$-C(O)OR^{PR}, -S-C(O)-$(CH_2)_4$-C(O)OH, -S-C(O)-$(CH_2)_5$-C(O)OH, -S-C(O)-$(CH_2)_5$-C(O)OR^{PR}, -S-C(O)-$(CH_2)_4$-C(O)OR^{PR}, -S-C(O)-CH(NH_2)-CH_2OH, -S-C(O)-CH_2-N(CH_3)-C(=NH)-NH_2, -S-C(O)-CH_2-NH-C(O)-CH(CH_2SH)-NH-C(O)-$(CH_2)_2$-CH(NH_2)-C(O)-OH), a C2-C20 such as -S-C(O)-CH_3, -S-C(O)-CF_3, -S-C(O)-CCl_3, -S-C(O)-C_2H_5, -S-C(O)-C_6H_5, -S-C(O)-C_6H_4-OCH_3, -S-C(O)-C_6H_4-F, -S-C(O)-C_6H_4-Cl, -S-C(O)-C_6H_4-CH_3, -S-C(O)-$C_{1\text{-}12}$ optionally substituted alkyl, -S-C(O)-CH_2-NHR^{PR}, -S-C(O)-CHOH-NHR^{PR}, -S-C(O)-CH[(CH(OH)(CH_3)]-NHR^{PR}, -S-C(O)-CH(CH_3)-NHR^{PR}, -S-C(O)-CH[$(CH_2)_2$C(O)OR^{PR}]-NHR^{PR}, -S-C(O)-CH(CH_2C(O)OR^{PR}-NHR^{PR}, -S-C(O)-CH[$(CH_2)_4NHR^{PR}$]-NHR^{PR}, -S-C(O)-CH[$(CH_2)_2$C(O)NHR^{PR}]-NHR^{PR}, -S-C(O)-CH(CH_2C(O)NHR^{PR})-NHR^{PR}, -S-C(O)-$(CH_2)_m$-C(O)O$N(R^{PR})_2$, -S-C(O)-$(CH_2)_m$-O-$(CH_2)_m$-C(O)OR^{PR}, -S-C(O)-$(CH_2)_m$-S-$(CH_2)_m$-C(O)OR^{PR}, -S-C(O)-$(CH_2)_m$-NR^{PR}-$(CH_2)_m$-C(O)OR^{PR}, -S-C(O)-$(CH_2)_m$-O-$(CH_2)_m$-C(O)O$N(R^{PR})_2$, -S-C(O)-$(CH_2)_m$-O-$(CH_2)_m$-C(O)O-C1-C10 optionally substituted alkyl, -S-C(O)-$(CH_2)_m$-O-$(CH_2)_m$-C(O)OR^{PR}, -S-C(O)-$(CH_2)_m$-S-$(CH_2)_m$-C(O)O-C1-C10 optionally substituted alkyl, -S-C(O)-$(CH_2)_m$-S-$(CH_2)_m$-C(O)OR^{PR}, -S-C(O)-$(CH_2)_m$-NR^{PR}-$(CH_2)_m$-C(O)O-C1-C10 optionally substituted alkyl, -S-C(O)-$(CH_2)_m$-NR^{PR}-$(CH_2)_m$-C(O)OR^{PR}, where the optionally substituted ~~alkyl optionally optionally is~~

~~methyl~~ alkyl optionally is methyl, ethyl, *i*-propyl, *n*-propyl, *t*-butyl, *n*-butyl, *n*-hexyl, *n*-octyl, *n*-decyl, vinyl, allyl, phenyl, $-CH_2OH$, $-CH_2F$, $-CF_2H$, $-(CH_2)_n-CH_3$, $-(CH_2)_n-OH$, $-(CH_2)_n-F$, $-(CH_2)_n-Br$, $-(CH_2)_n-NH_2$, $-(CH_2)_n-C(O)-OR^{PR}$, $-(CH_2)_n-O-CH_3$, $-(CH_2)_n-S-CH_3$, $-(CH_2)_m-(CH=CH)_p-(CH_2)_q-CH_3$, $-(CH_2)_m-(CH=CH)_p-(CH_2)_q-CH_2F$, $-(CH_2)_m-(CH=CH)_p-(CH_2)_q-CH_2Br$, $-(CH_2)_m-(CH=CH)_p-(CH_2)_q-C(O)-OR^{PR}$, $-(CH_2)_m-(CH=CH)_p-(CH_2)_q-NHR^{PR}$, $-CF_3$, $-CH_2CF_3$, $-C_2F_5$, or a thio analog of any ester moiety described herein, wherein R^{PR} independently are -H, a protecting group such as C1-C10 optionally substituted alkyl (e.g., $-CH_3$, $-C_2H_5$, $-C_3H_6OH$) or together are a protecting group, n is 1, 2, 3, 4, 5, 6, 7 or 8, m is 0, 1, 2, 3, 4, 5 or 6, p is 0 or 1 and q is 0, 1, 2, 3, 4, 5 or 6, or

Please replace paragraph 260 at page 74 with the following amended paragraph.

[00260] amino acid or peptide, e.g., a dipeptide, $-O-C(O)-CH_2-NHR^{PR}$, $-O-C(O)-CHOH-NHR^{PR}$, $-O-C(O)-CH[(CH(OH)(CH_3)]-NHR^{PR}$, $-O-C(O)-CH(CH_3)-NHR^{PR}$, $-O-C(O)-CH[(CH_2)_2C(O)OR^{PR}]-NHR^{PR}$, $-O-C(O)-CH(CH_2C(O)OR^{PR}-NHR^{PR}$, $-O-C(O)-CH[(CH_2)_4NHR^{PR}]-NHR^{PR}$, $-O-C(O)-CH[(CH_2)_2C(O)NHR^{PR}]-NHR^{PR}$, $-O-C(O)-CH(CH_2C(O)NHR^{PR})-NHR^{PR}$, $-O-C(O)-CHR^{42}-NHR^{PR}$, $-NH-(CH_2)_{1-4}-C(O)OR^{46}$ or $-O-C(O)-(CH_2)_{1-4}-NHR^{47}$ where R^{42} is -H, $-CH_3$, $-C_2H_5$, $-(CH_2)_n-C(O)-OR^{PR}$, $-CH_2-C(O)-OH$, $-CH_2-C(O)-NHR^{PR}$, $-CH_2F$, $-CH_2Cl$, $-CH_2Br$, $-CHOH-CH_3$ or $-CH_2OH$, R^{46} is -H, optionally substituted alkyl (e.g., $-CH_3$, $-C_2H_5$, $-C_2H_3$, $-C_3H_7$, $-C_3H_5$, $-(CH_2)_{1-8}-OH$, $-(CH_2)_{1-8}-NH_2$, $-(CH_2)_{1-8}-C(O)-OH$, $-(CH_2)_{0-3}-(CH=CH)_{0-1}-(CH_2)_{0-3}-CH_3$, $-(CH_2)_{0-3}-(CH=CH)_{0-1}-(CH_2)_{0-3}-CH_2F$, $-(CH_2)_{0-3}-(CH=CH)_{0-1}-(CH_2)_{0-3}-CH_2Br$, $-(CH_2)_{0-3}-(CH=CH)_{0-1}-(CH_2)_{0-3}-C(O)-OH$, $-(CH_2)_{0-3}-(CH=CH)_{0-1}-(CH_2)_{0-3}-NH_2$, $-CF_3$ or $-C_2F_5$) or a protecting group (e.g., *t*-butyl, phenyl, benzyl or substituted phenyl), R^{47} is -H, optionally substituted alkyl (e.g., $-CH_3$, $-C_2H_5$, $-C_2H_3$, $-C_3H_7$, $-C_3H_5$, $-(CH_2)_{1-8}-OH$, $-(CH_2)_{1-8}-NH_2$, $-(CH_2)_{1-8}-C(O)-OH$, $-(CH_2)_{0-3}-(CH=CH)_{0-1}-(CH_2)_{0-3}-CH_3$, $-(CH_2)_{0-3}-(CH=CH)_{0-1}-(CH_2)_{0-3}-CH_2F$, $-(CH_2)_{0-3}-(CH=CH)_{0-1}-(CH_2)_{0-3}-CH_2Br$, $-(CH_2)_{0-3}-(CH=CH)_{0-1}-(CH_2)_{0-3}-C(O)-OH$, $-(CH_2)_{0-3}-(CH=CH)_{0-1}-(CH_2)_{0-3}-$

NH_2, $-CF_3$ or $-C_2F_5$) or a protecting group (e.g., *t*-butyl, phenyl, benzyl or substituted phenyl) and R^{PR} is -H ~~or an indenendently selected protecting group~~ or an independently selected protecting group such as C1-C8 optionally substituted alkyl and n is 0, 1, 2, or 3, or

Please replace paragraph 316 at page 112 with the following amended paragraph.

[00316] Similarly, when R^1, R^2, R^3 and R^4 respectively are in the α,β,β,α configurations, group 14-3 compound 1.2.6.1 is 3α,7β,16β-trihydroxy-17α-aminoandrost-5-ene and group 14-3 compound 1.1.4.1 is 3α-hydroxy-16β-fluoro-17β-aminoandrost-5-ene. When R^1, R^2, R^3 and R^4 respectively are in the β,β,α,α configurations, group 14-3 compound 1.2.6.1 is 3β,7β,16α-trihydroxy-17α-aminoandrost-5-ene and group 14-3 compound 1.1.4.1 is 3β-hydroxy-16α-fluoro-17α-aminoandrost-5-ene. When R^1, R^2, R^3 and R^4 respectively are in the α,β,β,α configurations, group 14-4 compound 1.2.6.1 is 3α,7β,16β-trihydroxy-17α-aminoandrost-1,5-diene and group 14-4 compound 1.1.4.1 is 3α-hydroxy-16β-fluoro-17β-aminoandrost-1,5-diene. When R^1, R^2, R^3 and R^4 respectively are in the β,β,α,α configurations, group 14-4 compound 1.2.6.1 is 3β,7β,16α-trihydroxy-17α-aminoandrost-1,5-diene and group 14-4 compound 1.1.4.1 is 3β-hydroxy-16α-fluoro-17α-aminoandrost-1,5-diene. When R^1, R^2, R^3 and R^4 respectively are in the α,β,β,α configurations, group 14-2 compound 1.2.6.1 is 3α,7β,16β-trihydroxy-17α-amino-5β-androstane and group 14-2 compound 1.1.4.1 is 3α-hydroxy-16β-fluoro-17α-amino-5β-androstane. When R^1, R^2, R^3 and R^4 respectively are in the β,β,α,α configurations, group 14-2 compound 1.2.6.1 is 3β,7β,16α-trihydroxy-17α-amino-5β-androstane and group 14-2 compound 1.1.4.1 is 3β-hydroxy-16α-fluoro-17α-amino-5β-androstane. When R^1, R^2, R^3 and R^4 respectively are in the α,β,α,β configurations, group 14-2 compound 1.2.6.1 is 3α,7β,16α-trihydroxy-17β-amino-5β-androstane and group 14-2 compound 1.1.4.1 is 3α-hydroxy-16β-

fluoro-17β-amino-5β-androstane. When R^1, R^2, R^3 and R^4 respectively are in the β,β,β,α configurations, group 14-2 compound 1.2.6.1 is 3β,7β,16β-trihydroxy-17α-amino-5β-androstane and group 14-2 compound 1.1.4.1 is 3β-hydroxy-16β-fluoro-17α-amino-5β-androstane. ~~Compounds in other other groups~~ Compounds in other groups, e.g., groups 14-5, 14-5A, 14-6, 14-7, 14-8, 14-8A, 14-9, 14-10, 14-10A, 14-11, 14-12 or 14-13, where R^1, R^2, R^3 and R^4 respectively are in the listed configurations, e.g., α,β,α,β, β,β,β,α, β,β,α,α or β,β,β,β, are named or described in the same manner.

Please replace paragraph 334 at page 124 with the following amended paragraph.

[00334] **Group 21.** This group contains compounds in groups 1-20 above where R^4 substituents 1-10 listed in Table A are replaced with the following groups: 1 -optionally substituted amine, 2 -optionally substituted amide, 3 -optionally substituted oxime, 4 -optionally substituted alkyl, 5 -optionally substituted alkenyl, 6 -optionally substituted alkynyl, 7 -optionally substituted aryl, 8 -optionally substituted heterocycle, 9 -ether, e.g., methoxy, ethoxy or methoxymethyl and 10 -ester, e.g., acetate, propionate, *n*-butyrate, *i*-butyrate, *t*-butyrate, enanthate or trifluoroacetate. Any of these groups can be a moiety defined herein for that group. Thus, for Table A substituent 1, optionally substituted amine, the R^4 group includes any optionally substituted amine moieties described herein such as $-NH_2$, $-NH_3^+Cl^-$, $-NH_3^+Br^-$, $-NH_3^+I^-$, optionally substituted alkylamine, di-optionally substituted alkylamine, $-NHR^{PR}$, $-N(R^{PR})_2$, $-NH-CH_3$, $-N(CH_3)_2$, $-N(C_2H_5)_2$, -N(*n*-propyl)$_2$, -N(*i*-propyl)$_2$, -N(*n*-butyl)$_2$, -N(*t*-butyl)$_2$, $-NH-C_{1-4}$ alkyl, $-NH-C_{1-4}$ hydroxyalkyl, $-NH-C_{1-4}$ fluoroalkyl, $-NH-C_{5-8}$ alkyl, $-NH-C_{5-8}$ hydroxyalkyl, $-NH-C_{5-8}$ fluoroalkyl, $-NH-C_{5-8}$ $(halo)_n$-alkyl where n is 1, 2, 3, 4, 5, 6, 7 or 8 and the halogens are the same or different, $-NH-CH_2-CH_2-C(O)-OH$ or a salt, $-NH-CH_2-CH_2-C(O)-OCH_3$, $-NH-CH_2-CH_2-O-C(O)-OCH_3$ and $-NH-CH_2-CH_2-O-CH_3$, where R^{PR} are independently selected protecting groups and any alkyl group contains 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or

more carbon atoms and is optionally substituted as described herein. Similarly, optionally substituted amide includes moieties such as -C(O)-NH_2, -NH-C(O)-CH_3, -NH-C(O)-CF_3, -NH-C(O)-C_2H_5, -C(O)-NH-$C(CH_3)_3$ and -C(O)-NH_2, which are described herein. Other R^4 moieties include =N-OCH_3, =N-OC_2H_5, =N-OC_3H_7 and =N-O-optionally substituted alkyl, -NH_2, -$NHCH_3$, -$N(CH_3)_2$, -NHC_2H_5, -$N(C_2H_5)_2$, -NHC_3H_7, -$N(C_3H_7)_2$, -NHC_4H_9, -$N(C_4H_9)_2$, -NH-optionally substituted alkyl, -N(optionally substituted alkyl)$_2$, -NH-C_6H_5, -$N(C_6H_5)_2$, -NH-optionally substituted monosaccharide -NH-optionally substituted oligosaccharide, -NHC(O)-optionally substituted alkyl, -$N(CH_3)$-C(O)-optionally substituted alkyl, -$N(C_2H_5)$-C(O)-optionally substituted alkyl, -$N(C_3H_7)$-C(O)-optionally substituted alkyl, -$N(C_4H_9)$-C(O)-optionally substituted alkyl, -$N(C_6H_5)$-C(O)-optionally substituted alkyl, -NH-C(O)-optionally substituted monosaccharide and -NH-C(O)-optionally substituted oligosaccharide, where alkyl or phenyl groups are the ~~same or different and are optionally substitued~~ same or different and are optionally substituted as described herein.

Please replace paragraph 349 at page 133 with the following amended paragraph.

[00349] **Group 26.** This group contains compounds in groups 1-20 above where R^4 substituents 1-10 listed in Table A are replaced with the following groups: 1 -sulfonamide, 2 -sulfonamide derivative, e.g., -S(O)(O)-NHR^{PR} or -S(O)(O)-NH-optionally substituted alkyl, 3 -sulfamate, 4 -sulfamate derivative, e.g., -O-S(O)(O)-NHR^{PR}, -O-S(O)(O)-N(RD)$_2$ or -O-S(O)(O)-NH-optionally substituted alkyl, 5 -sulfonate, 6 -sulfamide, 7 -sulfinamide, 8 -sulfurous diamide, 9 -optionally protected monosaccharide, e.g., D-, L- or DL-glucose, galactose, fructose, rhamnose or glucuronic acid, 10 -optionally protected oligosaccharide, e.g., D-, L- or DL-galactose-galactose, -galactose-mannose or -glucuronic acid-glucose. In this group, the optionally protected monosaccharide and ~~optionally protected oligomonosaccharide moieties~~

optionally protected oligosaccharide moieties are typically linked to the 17-position through an oxygen, sulfur or nitrogen atom.

Please replace paragraph 361 at page 139 with the following amended paragraph.

[00361] **Group 28.** This group contains compounds in groups 1-27 above where R^1 substituents 1-10 listed in Table A are replaced with the following groups: 1 -optionally substituted amine, 2 -optionally substituted amide, 3 -optionally substituted oxime, 4 -optionally substituted alkyl, 5 -optionally substituted alkenyl, 6 -optionally substituted alkynyl, 7 -optionally substituted aryl, 8 -optionally substituted heterocycle, 9 -ether and 10 -ester. Any of these groups can be a moiety defined herein for that group. Thus, for Table A substituent 1, optionally substituted amine, the R^1 group includes moieties such as $-NH_2$, $-NH_3^+Cl^-$, $-NH_3^+Br^-$, $-NH_3^+I^-$, optionally substituted alkylamine, di-optionally substituted alkylamine, $-NH-CH_3$, $-N(CH_3)_2$, $-N(C_2H_5)_2$, -N(*n*-propyl)$_2$, -N(*i*-propyl)$_2$, -N(*n*-butyl)$_2$, -N(*t*-butyl)$_2$, $-NH-C_{1-4}$ alkyl, $-NH-C_{1-4}$ hydroxyalkyl, $-NH-C_{1-4}$ fluoroalkyl, $-NH-CH_2-CH_2-O-CH_3$, -NH-optionally substituted alkyl, -N(optionally substituted alkyl)$_2$, $-NH-C_6H_5$, $-N(C_6H_5)_2$, -NH-optionally substituted monosaccharide and -NH-optionally substituted oligosaccharide, and optionally substituted amide includes -NHC(O)-optionally substituted alkyl, $-N(CH_3)-C(O)$-optionally substituted alkyl, $-N(C_2H_5)-C(O)$-optionally substituted alkyl, $-N(C_3H_7)-C(O)$-optionally substituted alkyl, $-N(C_4H_9)-C(O)$-optionally substituted alkyl, $-N(C_6H_5)-C(O)$-optionally substituted alkyl, -NH-C(O)-optionally substituted monosaccharide and -NH-C(O)-optionally substituted oligosaccharide, where alkyl or phenyl groups are the same or different ~~and are optionally substituted as described herein~~ and are optionally substituted as described herein.

Please replace paragraph 369 at page 143 with the following amended paragraph.

[00369] **Group 33.** This group contains compounds in groups 1-27 above where R^1 substituents 1-10 listed in Table A are replaced with the following groups: 1 -sulfonamide, 2 -sulfonamide derivative, e.g., -S(O)(O)-NHR^{PR} or -S(O)(O)-NH-optionally substituted alkyl, 3 -sulfamate, 4 -sulfamate derivative, e.g., -O-S(O)(O)-NHR^{PR}, -O-S(O)(O)-$NHCH_3$, -O-S(O)(O)-NHC_2H_5, -O-S(O)(O)-NHC_3H_7, -O-S(O)(O)-NHC_4H_9, -O-S(O)(O)-$N(RD)_2$ or -O-S(O)(O)-NH-optionally substituted alkyl, 5 -sulfonate, 6 -sulfamide, 7 -sulfinamide, 8 -sulfurous diamide, 9 -optionally protected monosaccharide, e.g., D-, L- or DL-glucose, fructose, rhamnose or glucuronic acid, 10 -optionally protected oligosaccharide, e.g., D-, L- or DL-galactose-galactose, -galactose-mannose or -glucuronic acid-glucose. In this group, the optionally protected monosaccharide and ~~optionally protected oligomonosaccharide moieties~~ optionally protected oligosaccharide moieties are typically linked to the 3-position through an oxygen, sulfur or nitrogen atom.

Please replace paragraph 381 at page 149 with the following amended paragraph.

Please replace paragraph 381 at page 149 with the following amended paragraph.

[00381] **Group 35.** This group contains compounds in groups 1-34 above where R^3 substituents 1-10 listed in Table A are replaced with the following groups: 1 -optionally substituted amine, 2 -optionally substituted amide, 3 -optionally substituted oxime, 4 -optionally substituted alkyl, 5 -optionally substituted alkenyl, 6 -optionally substituted alkynyl, 7 -optionally substituted aryl, 8 -optionally substituted heterocycle, 9 -ether and 10 -ester. Any of these groups can be a moiety defined or described herein for that moiety, e.g., optionally substituted amine includes -NH_2, -$NH_3^+Cl^-$, -$NH_3^+Br^-$, -$NH_3^+I^-$, -$NHCH_3$, -$N(CH_3)_2$, -NHC_2H_5, -$N(C_2H_5)_2$, -NHC_3H_7, -$N(C_3H_7)_2$, -NHC_4H_9, -

$N(C_4H_9)_2$, -NH-optionally substituted alkyl, -N(optionally substituted alkyl)$_2$, -NH-C_6H_5, -$N(C_6H_5)_2$, -NH-optionally substituted monosaccharide and -NH-optionally substituted oligosaccharide, and optionally substituted amide includes -NHC(O)-optionally substituted alkyl, -$N(CH_3)$-C(O)-optionally substituted alkyl, -$N(C_2H_5)$-C(O)-optionally substituted alkyl, -$N(C_3H_7)$-C(O)-optionally substituted alkyl, -$N(C_4H_9)$-C(O)-optionally substituted alkyl, -$N(C_6H_5)$-C(O)-optionally substituted alkyl, -NH-C(O)-optionally substituted monosaccharide and -NH-C(O)-optionally substituted oligosaccharide, where alkyl or phenyl groups are the same or different and ~~are optionally substitued as described herein~~ are optionally substituted as described herein.

Please replace paragraph 388 at page 152 with the following amended paragraph.

[00388] **Group 40.** This group contains compounds in groups 1-34 above where R^3 substituents 1-10 listed in Table A are replaced with the following groups: 1 -sulfonamide, 2 -sulfonamide derivative, e.g., -S(O)(O)-NHR^{PR} or -S(O)(O)-NH-optionally substituted alkyl, 3 -sulfamate, 4 -sulfamate derivative, e.g., -O-S(O)(O)-NHR^{PR}, -O-S(O)(O)-$NHCH_3$, -O-S(O)(O)-NHC_2H_5, -O-S(O)(O)-NHC_3H_7, -O-S(O)(O)-NHC_4H_9, -O-S(O)(O)-N(RD)$_2$ or -O-S(O)(O)-NH-optionally substituted alkyl, 5 -sulfonate, 6 -sulfamide, 7 -sulfinamide, 8 -sulfurous diamide, 9 -optionally protected monosaccharide, e.g., D-, L- or DL-glucose, fructose, rhamnose or glucuronic acid, 10 -optionally protected oligosaccharide, e.g., D-, L- or DL-galactose-galactose, -galactose-mannose or -glucuronic acid-glucose. In this group, the optionally protected monosaccharide and ~~optionally protected oligomonosaccharide moieties are~~ optionally protected oligosaccharide moieties are typically linked to the 3-position through an oxygen, sulfur or nitrogen atom.

Please replace paragraph 392 at page 155 with the following amended paragraph.

[00392] **Group 40A.** This group contains compounds in groups 1-34 above where R^3 substituents 1-10 listed in Table A are replaced with the following groups: 1 -N-pyrrolidine, 2 -N1-pyrazolone, 3 -N2-pyrazolone, 4 -N-imidazolidin-2-one, 5 -N1-imidazole, 6 -N1-4,5-dihydroimidazole, 7 -N-morpholine, 8 -N1-pyridine, 9 -N-piperidine, 10 -N-piperazine. ~~The compounds inthis group~~ The compounds in this group are described as in other groups described above, e.g., group 40A-3 compound 1.1.1.9 (i.e., group 40A compound 1.1.1.9 from group 3) is 16α-N-pyrrolidiny-3β,17β-dihydroxyandrost-5-ene.

Please replace paragraph 400 at page 158 with the following amended paragraph.

[00400] **Group 42.** This group contains compounds in groups 1-41 above where R^2 substituents 1-10 listed in Table A are replaced with the following groups: 1 -optionally substituted amine, 2 -optionally substituted amide, 3 -optionally substituted oxime, 4 -optionally substituted alkyl, 5 -optionally substituted alkenyl, 6 -optionally substituted alkynyl, 7 -optionally substituted aryl, 8 -optionally substituted heterocycle, 9 -ether and 10 -ester. Any of these groups can be a moiety defined or described herein for that moiety, e.g., optionally substituted amine includes $-NH_2$, $-NH_3^+Cl^-$, $-NH_3^+Br^-$, $-NH_3^+I^-$, $-NHCH_3$, $-N(CH_3)_2$, $-NHC_2H_5$, $-N(C_2H_5)_2$, $-NHC_3H_7$, $-N(C_3H_7)_2$, $-NHC_4H_9$, $-N(C_4H_9)_2$, -NH-optionally substituted alkyl, -N(optionally substituted alkyl)$_2$, $-NH-C_6H_5$, $-N(C_6H_5)_2$, -NH-optionally substituted monosaccharide and -NH-optionally substituted oligosaccharide, and optionally substituted amide includes -NHC(O)-optionally substituted alkyl, $-N(CH_3)$-C(O)-optionally substituted alkyl, $-N(C_2H_5)$-C(O)-optionally substituted alkyl, $-N(C_3H_7)$-C(O)-optionally substituted alkyl, $-N(C_4H_9)$-C(O)-optionally substituted alkyl, -

$N(C_6H_5)$-C(O)-optionally substituted alkyl, -NH-C(O)-optionally substituted monosaccharide and -NH-C(O)-optionally substituted oligosaccharide, where alkyl or phenyl groups are the same or different and ~~are optionally substitued as described herein~~ are optionally substituted as described herein.

Please replace paragraph 407 at page 161 with the following amended paragraph.

[00407] **Group 47.** This group contains compounds in groups 1-41 above where R^2 substituents 1-10 listed in Table A are replaced with the following groups: 1 -sulfonamide, 2 -sulfonamide derivative, e.g., -S(O)(O)-NHR^{PR} or -S(O)(O)-NH-optionally substituted alkyl, 3 -sulfamate, 4 -sulfamate derivative, e.g., -O-S(O)(O)-NHR^{PR}, -O-S(O)(O)-$NHCH_3$, -O-S(O)(O)-NHC_2H_5, -O-S(O)(O)-NHC_3H_7, -O-S(O)(O)-NHC_4H_9, -O-S(O)(O)-$N(RD)_2$ or -O-S(O)(O)-NH-optionally substituted alkyl, 5 -sulfonate, 6 -sulfamide, 7 -sulfinamide, 8 -sulfurous diamide, 9 -optionally protected monosaccharide, e.g., D-, L- or DL-glucose, fructose, rhamnose or glucuronic acid, 10 -optionally protected oligosaccharide, e.g., D-, L- or DL-galactose-galactose, -galactose-mannose or -glucuronic acid-glucose. In this group, the optionally protected monosaccharide and ~~optionally protected oligomonosaccharide moieties~~ optionally protected oligosaccharide moieties are typically linked to the 3-position through an oxygen, sulfur or nitrogen atom.

Please replace paragraph 436 at page 179 with the following amended paragraph.

[00436] Embodiments include a method (the "characterization method") to characterize or at least partially characterize a formula 1 compound that is at least partially uncharacterized for one or more given chemical or analytical properties, e.g., a known or potential metabolite of a parent formula 1 compound, comprising (a) providing a formula 1 compound having one, two or

more known characteristics, e.g., a known or at least partially known or characterized chemical structure, XRD spectrum or melting point (a "CF1C"), and a formula 1 compound that is unknown or at least partially uncharacterized, i.e., ~~is uncharacerized for at least one of the same~~ is uncharacterized for at least one of the same analytical characteristics (a "UCF1C"), (b) obtaining one, two or more analytical characteristics of the UCF1C, and (c) comparing the 1, 2 or more analytical characteristics of the CF1C with the analytical characteristics of the UCF1C. The steps in this method may be conducted in any suitable order, e.g., analytical or chemical data for the CF1C will usually be obtained before or at about the same time as one obtains the analytical or chemical data for the UCF1C. Usually the CF1C will be more completely characterized than the UCF1C, particularly with regard to its chemical structure or its relative degree of purity or with regard to the analytical or chemical data that is being sought. This method allows further characterization of the UCF1C, e.g., by confirming the UCF1C's chemical structure or by determining the UCF1C's stability under various storage or temperature conditions or in various formulations or by determining other analytical or chemical properties of interest. In this method, the CF1C itself may not be completely characterized, however, for the one, two or more analytical characteristics of interest, the CF1C will usually have a known or confirmed property or properties, while the UCF1C is unknown or at least unconfirmed for the same property or properties.

Please replace paragraph 440 at page 181 with the following amended paragraph.

[00440] When characterizing a CF1C by MS, particularly by GC-MS, one will usually conduct an initial characterization of a formula 1 compound or a CF1C in the characterization method using a known GC-MS method (e.g., H.L.J. Makin et al., *Mass Spectra and GC Data of Steroids: Androgens and Estrogens* 1999 John Wiley & Sons, pages XIII-XIV) or a suitable variation of

this method. For F1Cs that contain free hydroxyls or oxo groups, the hydroxyl groups can be derivatized to an ester such as acetate, hydroxyl and oxo or groups can be derivatized to trimethylsilyl ether, i.e., -O-Si(CH_3)$_3$, and oxo groups can be derivatized to a an oxime such as =N-O-CH_3 before GC-MS analysis. Other functional groups can also be suitably derivatized. For embodiments of the characterization method that use a GC-MS analysis method, the CF1C or the UCF1C is analyzed by the GC-MS method or a suitable variation to obtain or to confirm chemical ~~structure information about the the CF1C~~ structure information about the CF1C or the UCF1C. Suitable variations include, e.g., a change in the carrier gas from helium to hydrogen to increase the sensitivity of detection or a decrease in the ionization from 70 eV to 50 eVcan give a better parent mass ion.

Please replace paragraph 458 at page 190 with the following amended paragraph.

[00458] Other embodiments comprise (1) administering a F1C(s) once every day (as a single dose or as 2 or 3 daily subdoses) for 3-15 or about 8-12 days, followed by (2) no dosing for 1, 2, 3, 4, 5, 6, 10, 15, 20, 25, 30, 35, 40, 45, 50, 56, 70, 84, 98, 112 or more days and then (3) administering the F1C(s) at least once more on one day, e.g., administering the F1C(s) once per day for about 3-15 or about 8-12 consecutive days essentially as described in step (1) and (4) optionally repeating steps (1), (2) and (3) 1, 2, 3, 4, 5 or 6 times or more. In a subset of these embodiments (1) comprises administering a F1C(s) once every day for about 5, 6, 7, 8, 9 or 10 days, followed by (2) no dosing for about 10-40 days, (3) administering the F1C(s) at least once more on one day, e.g., administering the F1C(s) once per day for about 10 days (4) repeating step (2) or a variation, e.g., no dosing for about 5-45 days, and (5) optionally repeating steps (1), (2), (3) and (4) or a variation thereof those steps 1, 2, 3, 4, 5 or 6 times or more, (5) administering by s.c. or i.m. injection of about 5-45 mg/kg/dose, about 6-43 mg/kg/dose or about 7-43 mg/kg/dose of a group 3

compound such as compound 1.1.5.9 in group 3 described below, once each 1, 2, 3, 4, 5, 6, 7, 8 or 10 days over a period of about 15-28 days, optionally beginning at about 1-72 hours after, about 1-48 hours after, about 1-24 hours after or about 24-72 hours after exposure of the subject to radiation or a cytotoxic chemotherapy, (6) ~~administering orally or by by~~ administering orally or by s.c. or i.m. injection about 0.5-10 mg/kg/dose, e.g., about 1.5-3 mg/kg/dose of a group 3 compound such as compound 1.1.5.1 described below, once each 1, 2, 3, 4, 5, 6, 7 or 8 days over a period of about 15-30 days, e.g., over a period of 12, 14, 15, 16, 17, 19, 20, 21, 22, 23, 24, 25, 26 or 32 days, optionally beginning at about 1-72 hours after, about 1-48 hours after, about 1-24 hours after or about 24-72 hours after exposure of the subject to radiation or a cytotoxic chemotherapy.

Please replace paragraph 481 at page 197 with the following amended paragraph.

[00481] Formulations suitable for parenteral delivery of F1Cs to subjects such as humans or animals typically comprise 1, 2, 3, 4, 5, 6 or more excipients. Exemplary embodiments include (1) any two, three or four of propylene glycol, PEG200, PEG300, ethanol, benzyl alcohol and benzyl benzoate and (2) any two, three or four of propylene glycol, PEG100, PEG200, PEG300, PEG400, benzyl alcohol and benzyl benzoate. Typically such formulations will contain both propylene glycol and one or more PEGs, e.g., PEG100, PEG200, PEG300 or PEG400, which ~~enhance the solublity of the F1C by a cosolvent effect~~ enhance the solubility of the F1C by a cosolvent effect.

Please replace paragraph 542 at page 223 with the following amended paragraph.

[00542] Hantavirus infection is a viral disease that rodents can transmit to humans and the infection is associated with serious lung or kidney infection. Symptoms of Hantavirus infection of the lungs include one or more of fever, muscle pain, myalgia, headache, abdominal pain, conjunctival bleeding, ~~diarrhea, orr coughing~~ diarrhea or coughing. Hantavirus kidney infection may be mild or severe and is associated with fever, headache, backache, abdominal pain, small bruise-like patches on the whites of the eyes, abdominal rash, impaired kidney function, nausea, loss of appetite, fatigue and intracranial bleeding.

Please replace paragraph 546 at page 225 with the following amended paragraph.

[00546] For any of the infections disclosed herein, a subject who has the infection, or is susceptible of developing the infection, e.g., by suspected or potential exposure to an infectious agent, is treated by ~~administering an effective amounf~~ administering an effective amount of a F1C to the subject. Such subjects may have, or be susceptible to developing another condition, e.g., an autoimmune condition, inflammation condition, cardiovascular condition or a cancer or precancer as described herein, such as rheumatoid arthritis, systemic lupus erythematosis, Crohn's disease, ulcerative colitis, type 1 diabetes, type 2 diabetes, peptic ulcers, skin ulcers, oral cavity ulcers, asthma, multiple sclerosis, coronary artery disease, ~~acute or chronic rheumatuc heart disease~~ acute or chronic rheumatic heart disease, atherosclerosis, stroke or lung cancer, that can be related to or exacerbated by the infection. In these embodiments, the F1Cs can function by one or more mechanisms, including enhancing innate immune responses, modulating, e.g., detectably increase or decrease, the level or activity of one or more of the transcription factors, enzymes or other biomolecules described herein, e.g., IL-1α, IL-1β, TNFα, TNF-β, IL-6, IL-8, IL-10, gro-α, IFN-γ, IFN-α, MCP-1, MIP-1α, MIP-1β, MIP-2, IP-10, LT-β, GM-CSF, RANTES or their isotypes or homologs

or cortisol. For example, molecules such as IL1α, TNFα, MIP-1α or MCP-1 are generally decreased in infections where there is an overexpression of one or more of these molecules. A detectable decrease of one or more of these molecules often occurs.

Please replace paragraph 554 at page 227 with the following amended paragraph.

[00554] In any of these bacterial infections, the subject is optionally treated with a suitable or appropriate antibacterial agent(s). Such agents include one, two or more antibacterial agents selected from an aminoglycoside, an amphenicol, an ansamycin, a β-lactam, a lincosamide, a macrolide, a peptide, a tetracycline, a 2,4-diaminopyrimidine, a nitrofuran, a quinolone, a sulfonamide, a sulfone, cycloserine, mupirocin and tuberin. Aminoglycosides include dihdrostreptomycin, gentamicin, kanamycin, neomycin, and streptomycin and the amphenicols include chloramphenicol and chloramphenicol palmitate. β-Lactams include cefadroxil, cefamandole, cefatrizine, cefazedone, cefazolin, cefixime, ceftibuten, ceftizoxime, cefuroxime, cephalexin, cephalosporin, cephalothin, amoxicillin, carbenicillin and a penicillin G. Macrolides or ~~other abtibiotics include~~ other antibiotics include clarithromycin, erythromycin, tetracycline, doxycycline, ciprofloxacin and dapsone.

Please replace paragraph 583 at page 240 with the following amended paragraph.

[00583] In treating endometriosis, the use of an F1C will slow the rate of disease progression and decrease the severity or frequency of one or more symptoms such as irregular menstrual periods, infertility abdominal pain or cramping and pain in the lower back or pelvic area, which may precede menstruation or may accompany sexual intercourse or bowel movements.

Beneficial effects from F1C treatment will be mediated in patients with endometriosis at least partially by increasing the patient's Th1 immune responses and/or by decreasing ~~anti-endometrial antibodies or aberrent~~ anti-endometrial antibodies or aberrant Th2 immune responses. Treatment of emdometriosis could be accompanied by other suitable treatments, e.g., treatment with one or more of estrogen, progesterone, danazol, follicle stimulating hormone antagonists, leutinizing hormone antagonists, gonadotropin-releasing hormone antagonists such as nafarelin acetate or analgesics such as codeine, tylenol or aspirin.

Please replace paragraph 586 at pages 241-242 with the following amended paragraph.

[00586] ~~In some of these embodimants~~ In some of these embodiments, the subject's hyperproliferation or malignant condition may be associated with or caused by one or more pathogens. Such conditions include hepatocellular carcinoma associated with HCV or HBV, Kaposi's sarcoma associated with HIV-1 or HIV-2, T cell leukemia associated with HTLV I, Burkitt's lymphoma associated with Epstein-Barr virus or papillomas or carcinoma associated with papilloma viruses (e.g., human HPV 6, HPV 11, HPV 16, HPV 18, HPV 31, HPV 45) or gastric adenocarcinoma, gastric MALT lymphoma or gastric inflammation associated with *Helicobacter pylori*, lactobacillus, enterobacter, staphylococcus or propionibacteria infection.

Please replace paragraph 596 at pages 246-247 with the following amended paragraph.

[00596] Exemplary symptoms that the use of the F1Cs can ameliorate include one or more of pain such as arm, jaw or chest pain, edema or swelling, high blood pressure, shortness of breath or dyspnea, e.g., on exertion or while prone, fatigue or malaise and low cardiac injection fraction. In treating a

cardiovascular condition in a subject or in improving one or more symptoms thereof, the F1Cs may accomplish one or more of increasing cardiac ejection volume or fraction, decreasing levels of IL-6, decreasing levels of C reactive protein, fibrinogen, cardiac creatinine kinase, increasing fatty acid ~~metabolism or utlization~~ metabolism or utilization by cardiac tissue, increasing carnityl palmitoyl fatty acid transferase or other cardiac metabolic enzymes, activating potassium dependent calcium channels, vasodilating or enhancing oxygen delivery to ischemic tissues or decreasing levels of scarring or plaque formation that occurs, e.g., after vascular damage. Symptoms associated with a cardiovascular condition such as ischemia that can be ameliorated also include acidosis, expression of one or more immediate early genes in, e.g., glial cells, vascular smooth muscle cells or endothelial cells, neuronal membrane depolarization and increased neuronal extracellular calcium and glutamate concentration. Other biological effects associated with treatment using a F1C may also be monitored, e.g., and increase or decrease of a cell surface antigen, a cytokine or an interleukin as disclosed herein.

Please replace paragraph 600 at pages 248-249 with the following amended paragraph.

[00600] Beneficial effects that can the F1Cs can exert on such related symptoms or conditions include improved glucose tolerance, improved glucose utilization, decreased severity or slowed progression of vascular disease (e.g., microvascular or macrovascular disease, including nephropathy, neuropathy, retinopathy, hypertension, cerebrovascular disease and coronary heart disease) or a decreased severity or slowed progression of atherosclerosis, an arteriosclerosis condition (e.g., coronary arteriosclerosis, hyperplastic arteriosclerosis, peripheral arteriosclerosis or hypertensive arteriosclerosis), decreased severity or slowed progression of diabetic osteoarthropathy, skin lesions, rhabdomyolysis, ketosis, detectably decreased generation of islet cell autoantibodies, decreased levels or activity of inflammatory macrophages

(foam cells) in atherosclerotic plaques, or detectably decreased expression or levels of one or more of human (or mammalian) angiopoietin-like 3 gene product, apolipoprotein C-1, inducible or constitutive nitric oxide synthase, e.g., in endothelial cells, macrophages or the like, pyruvate dehydrogenase kinase 4, carboxyl ester lipase, cholesteryl ester transfer protein, endothelial lipase, vascular wall lipoprotein lipase, anti-lipoprotein lipase autoantibodies, triglyceride-rich lipoproteins, LDL cholesterol, C-reactive protein, high sensitivity C-reactive protein, fibrinogen, plasma homocysteine, VCAM-1, IL-1 (e.g., IL-1β), IL-6, a TNF (e.g., TNFα), AP-1, NF-κB, and IFN-γ. In these any of these diseases or conditions, the F1Cs can also modulate, e.g., detectably increase, the activity or level of one, two or more of human (or mammalian) LOX-1, apolipoprotein A-1, apolipoprotein A-2, LPDL lipase, hormone sensitive lipase, paraoxonase, brain natriuretic peptide, a brain natriuretic peptide receptor, e.g., Npr1 or Npr3, hepatic lipase, LDL receptor, ~~HDL apoliporpotein E, HDL apoliporpotein J~~ HDL apolipoprotein E, HDL apolipoprotein J, HDL cholesterol, VLDL receptor, ATP-binding casette transporter 1, leukemia inhibitory factor, CD36, LXRα, LXRβ, CARβ, RXR, PPARα, PPARβ, PPARγ or a lipoprotein lipase, e.g., marophage lipoprotein lipase. As used herein, obesity includes a human with a body mass index of at least about 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36 or greater. Obese humans that are treated with a F1C may have one or more of the conditions descrbed here.

Please replace paragraph 727 at page 318 with the following amended paragraph.

[00727] R^{PR} independently is -H or a protecting group, optionally provided that (1) one or two of R^{10A}, R^{10B}, R^{10C}, R^{10D} and R^{10E} are not hydrogen or (2) one R^4 is $-NH_2$, ~~an opotionally substituted~~ an optionally substituted amine, $-N(R^{PR})^2$, =NOH, =NO-optionally substituted alkyl, an amide or an N-linked amino acid. In these embodiments, the subject may have or be subject to developing the listed condition and the subject can be a human or a primate.

Please replace paragraph 818 at page 333 with the following amended paragraph.

[00818] 54. The method ~~of any preceeding~~ of any preceding embodiment wherein R^7 is $-CH_2-$, -C(α-OH, β-H)-, -C(β-OH, α-H)- or -C(O)-.

Please replace paragraph 819 at page 333 with the following amended paragraph.

[00819] 55. The method ~~of any preceeding~~ of any preceding embodiment wherein R^8 is $-CH_2-$, -C(α-OH, β-H)-, -C(β-OH, α-H)-, -C(α-OH, β-F)-, -C(β-OH, α-F)-, -C(α-F, β-H)-, -C(β-F, α-H)- or -C(O)-.

Please replace paragraph 820 at page 333 with the following amended paragraph.

[00820] 56. The method ~~of any preceeding~~ of any preceding embodiment wherein R^9 is $-CH_2-$, -C(α-OH, β-H)-, -C(β-OH, α-H)- or -C(O)-.

Please replace paragraph 821 at page 334 with the following amended paragraph.

[00821] 57. The method ~~of any preceeding~~ of any preceding embodiment wherein R^{10A} is -H, α-OH, β-OH or =O.

Please replace paragraph 822 at page 334 with the following amended paragraph.

[00822] 58. The method ~~of any preceeding~~ of any preceding embodiment wherein R^{10B} is -H, α-OH, β-OH or =O.

Please replace paragraph 823 at page 334 with the following amended paragraph.

[00823] 59. The method ~~of any preceeding~~ of any preceding embodiment wherein R^{10C} is -H, α-OH, β-OH or =O.

Please replace paragraph 824 at page 334 with the following amended paragraph.

[00824] 60. The method ~~of any preceeding~~ of any preceding embodiment wherein R^{10D} is -H, α-OH, β-OH or =O.

Please replace paragraph 825 at page 334 with the following amended paragraph.

[00825] 61. The method ~~of any preceeding~~ of any preceding embodiment wherein R^{10E} is -H, α-OH, β-OH or =O.

Please replace paragraph 826 at page 334 with the following amended paragraph.

[00826] 62. The method ~~of any preceeding~~ of any preceding embodiment wherein R^4 are (α-OH, β-H), (β-OH, α-H), (α-$C(O)CH_3$, β-H), (β-$C(O)CH_3$, α-H), (α-OH, β-F), (β-OH, α-F), (α-H, β-F), (β-H, α-F), (α-NH_2, β-H), (β-NH_2, α-H), =O, $=CH_2$ or $=CH-CH_3$.

Please replace paragraph 827 at page 334 with the following amended paragraph.

[00827] 63. The method ~~of any preceeding~~ of any preceding embodiment wherein R^1 are (H, H), (α-OH, β-H), (β-OH, α-H) or =O.

Please replace paragraph 828 at page 334 with the following amended paragraph.

[00828] 64. The method ~~of any preceeding~~ of any preceding embodiment wherein R^2 are (H, H), (α-OH, β-H), (β-OH, α-H) or =O.

Please replace paragraph 829 at page 334 with the following amended paragraph.

[00829] 65. The method ~~of any preceeding~~ of any preceding wherein R^3 are (H, H), (α-OH, β-H), (β-OH, α-H), (α-H, β-F), (β-H, α-F) or =O.

Please replace paragraph 831 at page 336 with the following amended paragraph.

[00831] 67. A method to treat, ameliorate or slow the progression of cystic fibrosis in a human comprising administering to the human an effective amount of a formula 1 compound ~~of any preceeding~~ of any preceding embodiment.

Please replace paragraph 836 at pages 336-337 with the following amended paragraph.

[00836] 72. A method to prevent, treat or ameliorate neutropenia in a human comprising administering to the human an effective amount of a formula 1 compound of any of embodiments 1-66, wherein the neutropenia is postinfectious neutropenia, autoimmune neutropenia, chronic idiopathic neutropenia or a neutropenia resulting from or potentially resulting result from

a cancer chemotherapy, chemotherapy for an autoimmune disease, an antiviral therapy, radiation exposure, tissue or solid organ allograft or xenograft rejection or immune suppression therapy in tissue or solid organ transplantation ~~or aging or immunesenescence~~ or aging or immune senescence.

Please replace paragraph 841 at page 338 with the following amended paragraph.

[00841] 77. The compound of embodiment 76 wherein one R^3 is a halogen, the other R^3 is not a halogen and one R^4 is $-NH_2$, ~~a subtituted amine~~ a substituted amine, an N-linked amino acid, $-N(R^{PR})_2$ or an amide, where R^{PR} independently or together are -H or a protecting group.

Please replace paragraph 849 at page 340 with the following amended paragraph.

[00849] 83. The method of embodiment 81 or 82 wherein the level or activity of IgE in the subject is at least transiently detectably reduced, e.g., shortly after allergen exposure (such as within about 1 hour to about 1 week) ~~or at one mor more later times~~ or at one or more later times.

Please replace paragraph 855 at page 341 with the following amended paragraph.

[00855] 88. A method to increase the efficacy of allergy vaccinations in a subject having an allergy, comprising (1) at an effective time before or during vaccination of the subject with an allergen, administering to the subject an effective amount of a formula 1 compound of embodiment 1, (2) optionally administering to the subject an effective amount of the formula 1 compound daily or intermittently for 2, 3, 4, 5, 6, 7, 14 or more days ~~after the vacination of~~

~~step~~ after the vaccination of step (1), (3) after passage of sufficient time, repeating step (1) and (4) after passage of sufficient time, optionally repeating steps (1), (3) and/or (2).

Please replace paragraph 883 at page 348 with the following amended paragraph.

[00883] 113. The method of embodiment 109 wherein the subject has experienced an immune suppressive ~~event within within~~ event within 3 weeks of the occurrence of the trauma or acute injury, wherein the immune suppressive event is selected from an immune suppressive amount of an immunosuppressive chemotherapy.

Please replace paragraph 884 at page 348 with the following amended paragraph.

[00884] 114. The method of embodiment 113 wherein the immunosuppressive chemotherapy is an immunosuppressive cancer chemotherapy, an immunosuppressive ~~amtimicrobial therapy~~ antimicrobial therapy or an immunosuppressive glucocorticoid therapy.

Please replace paragraph 902 at page 351 with the following amended paragraph.

[00902] 130. The use of a compound, composition, formulation or product of any of embodiments 1-129 or of any species or group of F1Cs disclosed herein to prepare a medicament for use to prevent or to treat, or to ameliorate one or more symptoms associated, with one, two or more acute or chronic diseases or conditions disclosed herein, e.g., an infection, ~~an immunesuppression condition~~ an immune suppression condition, an allergy, a cardiovascular condition, a metabolic disorder, a pulmonary condition, a skin

condition, aging, a trauma such as a burn or a bone fracture, immune suppression, a neurological ~~or centeral or peripheral~~ or central or peripheral nervous system condition or disorder, an unwanted or pathological inflammatory condition, toxicity or unwanted side-effects of a ~~chemotherapy orof radiation~~ chemotherapy or of radiation exposure such as a glucocorticoid treatment or a cancer chemotherapy, an autoimmune disease or condition, a malignancy or cancer, a pre-malignant condition or to modulate a mammal's immune response, such as enhancing a Th1 response or decreasing a Th2 response, in a subject, e.g., a human or a mammal, having the acute or chronic disease or condition or subject to developing the acute or chronic disease or condition.

Please replace paragraph 905 at page 352 with the following amended paragraph.

[00905] 133. Use of a compound, composition, formulation or product of any of embodiments 1-129 or of any species or group of F1Cs disclosed herein to prepare a medicament for use ~~to enhacnce a specific~~ to enhance a specific or an innate humoral or cellular response to vaccination or to the presence of 1, 2, 3, 4, 5, 6 or more endogenous antigens or epitopes associated with establishing or maintaining a disease or pathogenic agent such as a tumor antigen or an antigen associated with a pathogen.

Please replace paragraph 907 at page 352 with the following amended paragraph.

[00907] 135. Use according to embodiment 13 or 134 wherein the subject's innate or adaptive immunity is enhanced or wherein an unwanted immune response is decreased, or wherein number or activity of one, two or more of the subject's Th1 cells, tumor-infiltrating lymphocytes (TIL cells), NK cells, peripheral blood lymphocytes, phagocytes, monocytes, macrophage,

neutrophils, eosinophils, dendritic cells, fibrocytes, astrocytes, ~~gilal cells or stromal cells~~ glial cells or stromal cells, e.g., bone marrow, lymph node or spleen stroma, are increased or activated at least transiently (e.g., for at least 10 minutes to 10 days or more), which is optionally as measured by, e.g., enhanced ^{3}H-thymidine uptake compared to untreated controls or by an increase in the number of the cell type in circulation or demonstrable movement of the cell type from one tissue or compartment (e.g., skin or blood) to another tissue or compartment (e.g., blood, lymph node, spleen, Peyer's patches, GALT or thymus), or wherein the transcription rate, protein level or biological activity of one or more genes in the subject's NK cells, TIL cells, phagocytes, monocytes, macrophages, neutrophils, eosinophils, dendritic cells, fibrocytes, astrocytes, ~~gilal cells or stromal cells~~ glial cells or stromal cells are detectably modulated, e.g., increased (e.g., as measured by increased enzyme or biological activity of a biomolecule such as a nuclear hormone receptor such as an orphan nuclear hormone receptor, a transcription factor, a chemokine or a cytokine, which is optionally compared to suitable control cells or tissues).

Please replace paragraph 919 at page 356 with the following amended paragraph.

[00919] **Example 2.** Treatment of ionizing radiation exposure. The effect of selected F1Cs on survival of lethally-irradiated female B6D2F1 mice were compared to control animals treated with vehicle alone. The animals were exposed to 10 Gy of total body irradiation at 2.5 Gy/min using a ^{137}Cs source. Groups of 12 animals were used in a total of 5 groups. For Groups 1, 2, 3, and 5, test article was administered as a 100 μL volume, by subcutaneous injection, for three consecutive days, with the first dose administered 2 to 4 hours following exposure to radiation. For Group 4, test article was administered as a 50 μL volume, by intramuscular injection for three consecutive days. The ~~formulation was a a suspension~~ formulation was a

suspension containing 0.1% w/v carboxymethyl-cellulose, 0.9% w/v sodium chloride and 0.05% v/v phenol. The formulations were agitated to uniformly resuspend the F1C before syringing, and injected into animals within a few minutes of drawing into the syringe.

Please replace paragraph 924 at page 358 with the following amended paragraph.

[00924] The number of surviving and/or regenerating intestinal crypts in each treatment group, and the control groups, are scored. The mean number of crypts per cross-section in each group is determined. Surviving crypt widths is measured to correct for size-induced scoring anomalies. For each mouse, about 10 cross-sections of ~~intestine is analysed~~ intestine is analyzed (see, e.g., C.S. Potten et al., *Cell Proliferation* 36:115-129 2003) to obtain the numbers of repopulating intestinal crypts. The capacity of the F1C to enhance repopulation is observed as increased numbers of repopulating crypts in animals treated with a F1C ~~compared to irradiated controls~~ compared to irradiated controls. F1Cs such as one or more of 3β-hydroxy-17β-aminoandroat-5-ene, 3α-hydroxy-17β-aminoandroat-5-ene, 3β-hydroxy-17β-aminoandroat-1,5-diene, 3α-hydroxy-17β-aminoandroat-1,5-diene, 3β,17β-dihydroxyandroat-5-ene, 3β,17β-dihydroxy-16α-haloandroat-5-ene and 3β,17β-dihydroxy-16α-haloandroat-1,5-diene are tested.

Please replace paragraph 925 at pages 358-359 with the following amended paragraph.

[00925] **Example 5.** Human and primate virus treatment protocol. Humans infected with a virus, e.g., HCV, HBV or a retrovirus such as HIV1 or HIV2 or primates infected with a virus such as HCV, HIV1, HIV2, SIV or $SHIV_{229}$ are treated with a F1C formulation. Daily dosages of about 0.05 to about 25 mg/kg ~~are admnistered daily~~ are administered daily or on an

intermittent basis. The F1C is administered, e.g., orally, by subcutaneous injection, by intramuscular injection or by transmucosal delivery. A typical intermittent dosing protocol for human patients comprises daily dosing of about 0.1-5 mg/kg of the F1C for 1, 2, 3, 4, 5 or 6 days, followed by no dosing for about 1, 2, 3, 4, 5, 6, 7 or 8 weeks, daily dosing again for 1, 2, 3, 4, 5 or 6 days, no dosing for about 1, 2, 3, 4, 5, 6, 7 or 8 weeks and optionally repeating this dosing schedule as desired, e.g., for 3, 4, 5, 10, 15 or more rounds of dosing. A related dosing protocol involves dosing on every 2nd or 3rd day to deliver 2, 3, 4, 5 or 6 doses of the F1C, no dosing for about 2, 3, 4, 5, 6, 7 or 8 weeks and optionally repeating this dosing schedule as desired, e.g., for 3, 4, 5, 10, 15 or more rounds of dosing. Typical daily F1C doses in human treatment protocols is about 5 mg to about 1000 mg, usually about 10-150 mg. Daily doses can vary depending on the route of F1C administration and on the patient's weight and clinical condition, with oral administration usually requiring higher daily doses than parenteral or transmucosal administration.

Please replace paragraph 930 at page 360 with the following amended paragraph.

[00930] **Example 7.** Stimulation of phagocytosis. The capacity of F1Cs to influence phagocytosis of *Plasmodium* parasite-infected RBC is examined using adherent human monocytes. The parasitemia level is about 8-10% and human monocytes are obtained from buffy coats from blood as follows. Peripheral blood mononuclear cells are separated from freshly collected platelet-poor buffy coats discarded from blood samples of ~~heafthy adult donors~~ healthy adult donors of both sexes. Separated cells are washed once with luke-warm PBS supplemented with 10 mM glucose (PBS-G) and resuspended at 5 x 10^6 cells/mL in ice-cold RPMI 1640 medium supplemented with 23 mM $NaHCO_3$ and 25 mM Hepes, pH 7.4 (RMBH). Dynabeads M450 Pan B and Pan T (Dynal) are added to cells in a 4:1 ratio for 20 min at 4°C. B-lymphocytes and T-lymphocytes are removed as specified by the

manufacturer. The remaining monocytes are washed 2 times in RMBH, resuspended in AIM V cell culture medium (Gibco) at 1 x 10^6 cell/mL. The monocyte layer is collected, washed with PBS-G at 37°C and resuspended in AIM V medium at 1 x 10^6 cells/mL. Purified cells are >90% monocytes as assessed by CD14 expression.

Please replace paragraph 931 at pages 360-361 with the following amended paragraph.

[00931] Phagocytosis of opsonized parasitized RBC (PE) is determined as follows. Phagocytosis of fresh-serum opsonized PE is initiated by mixing 10 PE/monocyte. Suspensions are briefly centrifuged (150 x g for 5 sec at room temperature) to improve contact between PE and monocytes. ~~To avoid attachement~~ To avoid attachment of monocytes after centrifugation and during the whole incubation period, cells are kept in suspension at 5 x 10^6 cells/5 mL AIM V medium in 6 cm diameter teflon bottom dishes (Heraeus) in a humidified incubator (95% air, 5% CO_2) at 37°C. On average, at least 90% of the monocytes phagocytose PE, as assessed by microscopic inspection. Control cells are kept under similar conditions without phagocytosis. Quantitative assessment of phagocytosis is performed by a previously described bioluminescence method (E. Schwarzer, et al., *Br. J. Haematol.* 1994 88: 740-745).

Please replace paragraph 934 at pages 361-362 with the following amended paragraph.

[00934] **Example 8.** Cyclodextrin formulation. A cyclodextrin formulation containing a F1C is prepared by mixing a sulfobutyl β-cyclodextrin and the F1C in one or more liquids such as ethanol, DMSO, N-methylpyrrolidine, pyridine or water. The sulfobutyl β-cyclodextrin contains one or more butyl sulfonate or -O-$(CH_2)_4$-$SO_3^-Na^+$ moieties, typically about 5, 6 or 7 per cyclodextrin molecule.

F1Cs that contain a positive charge are especially helpful in forming complexes with the multiple negative charges of sulfobutyl cyclodextrin. For parenteral formulations, the maximum concentrations could be achieved at about the maximum cyclodextrin concentration that is still syringable, about 50% w:v. The F1C can be added to a solution of sulfobutyl β-cyclodextrin at a molar ratio of about 1:1, e.g., 0.5:1 to about 2:1, and stirred with or without heat for up to about 1 week to form the complex. The solution is optionally filtered or sterilized before filling in vials or injection delivery by any route. The vials can be sterilized by radiation ~~or by sterilie filtration~~ or by sterile filtration. An exemplary preparation is made using 500 grams of sulfobutyl β-cyclodextrin (about 230 mmoles) combined with about 230 mmoles of the F1C. Solutions containing about 20-80 mg/mL of the F1C are typically obtained. For pharmaceutical formulations, the complex is prepared under GMP compliance conditions. The dried complex is prepared by lyophilization and can be reconstituted, e.g., using sterile 0.9% NaCl. The cyclodextrin complex can also be dried for preparation of formulations for oral or transmucosal administration or reconstituted with water for parenteral delivery, e.g., by subcutaneous or intramuscular injection. F1Cs that are used include 3β,17β-dihydroxyandrost-5-ene, 3β,17β-dihydroxy-16α-fluoroandrost-5-ene, 3β,7β,17β-trihydroxyandrost-5-ene, 3β-hydroxy-3α-methyl-17β-aminoandrost-4-ene, 3α-hydroxy-3β-methyl-17β-aminoandrost-4-ene and 3β-hydroxy-17β-aminoandrost-5-ene.

Please replace paragraph 942 at page 364 with the following amended paragraph.

[00942] Treatment of aged, vaccinated animals ~~with the F1Cs,~~ with the F1Cs can result in higher anti-HbsAg IgG titers than aged animals receiving the vaccination only. Such results would show that the F1Cs can enhance immune response to antigen challenge in immune senescent animals.

Please replace paragraph 944 at page 364 with the following amended paragraph.

[00944] To examine the secondary antibody response, 42 days after the initial exposure to HbsAg, serum samples are taken from the mice and these are tested for anti-HbsAg IgG. At this time-point, vaccine-specific IgG titers are either low or undetectable. Three days later (45 days after first vaccination), the mice are injected again with HbsAg in alum, but this time, none of the mice receive any F1C (secondary vaccination). Serum samples collected 7 days and 14 days after the second exposure to HbsAg vaccine are assayed for anti-HbsAg antibody. In the young mice, a marked increase in specific antibody is seen in response to the second vaccination. In aged mice ~~that had receive no~~ that had received no F1C with the first HbsAg injection, levels of anti-HbsAg are measured. The data is analyzed for increases in anti-HbsAg titers following secondary vaccination in aged animals that had been treated with a F1C in conjunction with the first HbsAg exposure.

Please replace paragraph 945 at pages 364-365 with the following amended paragraph.

[00945] **Example 12.** Vaccine adjuvant activity. Selected F1Cs are used to modulate the immune response to an antigen(s) such as malaria antigens encoded by DNA expression vectors. Antigens such as a *Plasmodium*, e.g., *P. yoelii, P. falciparum, P. vivax* or *P. berghei*, circumsporozoite or merozoite protein are used to immunize a subject. The F1C is administered on the same day or a day or two before antigen challenge. Suitable antigens, expression vectors and their delivery to a subject have been described. See, e.g., S.L. Hoffman et al., *Vaccine* 1994 12:1529-1533, R. Weiss et al., *Infect. Immunity* 2000 68:5914-5919, J.C. Rayner et al., *Proc. Nat'l. Acad. Sci. U.S.A.* 2000 97:9648-9653, S. Scheiblhofer et al., *Eur. J. Immunol.* 2001 31:692-298. The capacity of the ~~compounds to enahnce immune responses~~ compounds to

enhance immune responses to the antigens by, e.g., measuring cytotoxic T lymphocytes or antibody titer after delivery of the formula 1 compound and immunization with an antigen(s). Typically the immune response is measured at about 10 days to about 21 days after a primary immunization. Methods to measure immune responses are essentially as described herein or in appropriate cited references. DNAs that encode an antigen(s) that is associated with, e.g., an infectious agent or a tumor described herein may be used in these assays.

Please replace paragraph 946 at page 365 with the following amended paragraph.

[00946] Example 13. ~~Supression of TNF-α induced adhesion~~ Suppression of TNF-α induced adhesion molecule expression. The recruitment of lymphocytes to areas of inflammation and angiogenesis involves specific receptor-ligand interactions between cell surface adhesion molecules (CAMs) on lymphocytes and the vascular endothelium. The adhesion process, in both normal and pathological settings, follows a multi-step cascade that involves intercellular adhesion molecule-1 (ICAM-1), vascular cell adhesion molecule-1 (VCAM-1), and endothelial leukocyte adhesion molecule-1 (E-selectin) expression on endothelial cells (EC). The expression of these molecules and others on the vascular endothelium determines the efficiency with which leukocytes may adhere to the local vasculature and extravasate into the local tissue during the development of an inflammatory response. The local concentration of cytokines and growth factor participate in the modulation of the expression of these CAMs.

Please replace paragraph 948 at page 366 with the following amended paragraph.

[00948] HUVECs are grown in a standard 96 well plate to confluence. Growth medium is removed from the cells and replaced with 90 μL of 199 Medium (10% FBS). Samples for testing and positive or negative controls are added to the plate in triplicate (in 10 μL volumes). Plates are incubated at 37ºC for either 5 h (selectin and integrin expression) or 24 h (integrin expression). Plates are aspirated to remove medium and 100 pL of 0.1% paraformaldehyde-PBS (with Ca^{++} and Mg^{++}) is added to each well. Plates are held at 4°C for 30 min. Fixative is then removed from the wells and wells are washed 1X with PBS(+Ca,Mg)+0.5% BSA and drained. Do not allow the wells to dry. 10 pL of diluted primary antibody is added to the test and control wells. Anti-ICAM-1-Biotin, Anti-VCAM1-Biotin and Anti-E-selectin-Biotin are used at a concentration of 10 pg/ml (1:10 dilution of 0.1 mg/ml stock antibody). Cells are incubated at 37°C for 30 min. in a humidified environment. Wells are washed X3 with PBS (with Ca, Mg) and 0.5% BSA. Then add 20 pL of diluted ~~ExtrAvidin- Alkaline Phosphotase~~ ExtrAvidin-Alkaline Phosphatase (1:5,000 dilution) to each well and incubate at 37ºC for 30 min. Wells are washed X3 with PBS (with Ca, Mg) and 0.5% BSA. 1 tablet of p-Nitrophenol Phosphate pNPP is dissolved in 5 mL of glycine buffer (pH 10.4). ~~100 pl of pNPP substrate in glycine buffer~~ 100 pL of pNPP substrate in glycine buffer is added to each test well. Standard wells in triplicate are prepared from the working dilution of the ~~ExtrAvidin-Alkaline Phosphotase~~ ExtrAvidin-Alkaline Phosphatase in glycine buffer: 5 pL of each dilution is added to triplicate wells and the resulting AP content in each well is 5.50 ng, 1.74 ng, 0.55 ng, 0.18 ng. 100 pl of pNNP reagent is then be added to each of the standard wells. The plate is incubated at 37ºC for 4h. A volume of 50 pL of 3M NaOH is added to all wells. The results are quantified on a plate reader at 405 nm. The background subtraction option is used on blank wells filled with glycine buffer only. The template is set up to indicate the concentration of AP-conjugate in each standard well. Results are indicated as amount of bound APconjugate in each sample.

Please replace paragraph 959 at page 370 with the following amended paragraph.

[00959] **Example 17.** ~~Hematopoiesis modulaton~~ Hematopoiesis modulation. Enhanced hematopoiesis is observed in mammals with immune injury from, e.g., radiation exposure or from an immunosuppressive chemotherapy. In an example, animals are used to demonstrate the effect of formula 1 compounds on hematopoiesis after immune system injury due to radiation. Hematopoiesis in the murine immune system after radiation is optionally used because of the similar responses of murine and human hematopoiesis to drugs and toxic insults (see, e.g., J.H. Hendry and B.I. Lord, editors, *Radiation toxicology: Bone marrow and leukaemia* 1995 Taylor & Francis Inc., London).

Please replace paragraph 961 at pages 371-371 with the following amended paragraph.

[00961] Mice are placed in ventilated Plexiglas containers and exposed bilaterally to gamma-radiation from a ^{60}Co source. Exposure time is adjusted so that each animal received a midline tissue-absorbed dose of 1-12 Gy at a nominal dose rate of 0.4 Gy/min at ambient temperature. Using a standardized technique, the midline dose rate is measured by placing a 0.5 cc tissue-equivalent ionization chamber at the center of a 2.5-cm diameter cylindrical acrylic mouse phantom. The tissue-air ratio, defined as the ratio of the dose rate measured in the phantom to the dose rate in free air, for this array is about 0.96. Variation within the exposure field is less than about 4%. Dosimetric measurements are made in accordance with the American Association of Physicists in Medicine protocol for the determination of absorbed dose from high-energy photon and electron beams (*Med. Phys.* 1983 10:741-771). Sham-irradiated mice are treated in the same way as the

irradiated animals, except that ~~the animals are not irridiated~~ the animals are not irradiated.

Please replace paragraph 966 at page 372 with the following amended paragraph.

[00966] . For induced-infection studies, a clinical isolate of K. *pneumoniae,* capsule type 5 (strain AFRRI 7), that is kept frozen at 70 °C in skim milk, is grown overnight at 35 °C on Trypticase Soy Agar (Becton-Dickinson, Sparks, MD). Five typical colonies are inoculated into 8 mL of brain heart infusion broth (Becton-Dickinson) and incubated overnight at 35 °C. Two milliliters of this overnight suspension is inoculated into 95 mL of prewarmed brain heart infusion broth. The culture is incubated at 35 °C with shaking for approximately 2.5 h. The optical density of bacterial growth is monitored with a spectrophotometer at a wavelength of 550 nm. Late log-phase cells are ished and suspended in cold saline to yield 10^9 viable bacteria per mL. Appropriate dilutions for inoculations are made in cold saline.

Please replace paragraph 9674 at page 374 with the following amended paragraph.

[00974] Effects of formula 1 compounds and Hydrocortisone on Proliferation in the Presence of a Mitogen. A series of spleen cell cultures is run using a formula 1 compound and/or hydrocortisone with cell cultures to which concanavalin A is added. Preliminary tests on cultures to which concanavalin A is added at concentrations of 10.0, 5.0, 2.5 and 1.0 ng/mL. All tests on the effects of invention compounds on cultures stimulated with concanavalin A are performed with concanavalin A at, e.g., about 2.5 ng/mL. A mitogen such as ConA generally increases cell proliferation and the glucocorticoid steroid ("GCS") can decrease proliferation. Detectable partial or

complete reversal of the inhibitor effects of hydrocortisone ~~indicate an anti-glucorticoid~~ indicate an anti-glucocorticoid effect by the formula 1 compounds.